

Claims

1. A method of preparing a phenotypically antibiotic-resistant subpopulation of stationary phase bacteria comprising at least the steps of:

(i) growing a bacterial culture to stationary phase; and

(ii) treating said stationary phase culture with one or more antibacterial agents at a concentration and for a time sufficient to kill growing bacteria, thereby selecting a phenotypically antibiotic-resistant subpopulation.

2. A method as claimed in claim 1 wherein said antibacterial agent is selected from the group consisting of: rifampicin, kanamycin, ampicillin and pyrazinamide.

3. A method as claimed in claim 1 or 2 wherein said antibacterial agent is used at a concentration of 25 to 150 µg/ml with bacteria present at a concentration of 10^5 to 10^9 bacteria/ml.

4. A method as claimed in any one of claims 1 to 3 wherein said bacteria are *Staphylococcus aureus*, *Eschericia coli*, *Haemophilus influenzae*, *Streptococcus pyogenes*, *Streptococcus gordonii* or *Mycobacterium tuberculosis*.

5. A method as claimed in any one of claims 1 to 4 wherein said bacteria are *Mycobacterium tuberculosis* and said antibacterial agent is rifampicin.

6. A method as claimed in any one of claims 1 to 4 wherein said bacteria are *Eschericia coli* and said antibacterial agent is kanamycin.

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Sub A2 7. A method as claimed in any one of claims 1 to 4 wherein said bacteria are *Staphylococcus aureus* and said antibacterial agent is ampicillin.

5 8. A phenotypically antibiotic-resistant subpopulation of stationary phase bacteria, obtainable by a method as defined in any one of claims 1 to 7.

10 9. A process for assessing the antibacterial activity of a test compound or agent or for isolating a compound or agent having antibacterial activity against stationary phase bacteria comprising the steps of:

15 (i) preparing a phenotypically antibiotic-resistant subpopulation of stationary phase bacteria according to the method defined in any one of claims 1 to 7;

(ii) incubating a sample of said phenotypically resistant subpopulation with one or more test compounds or agents; and

20 (iii) assessing any antibacterial effects against said phenotypically resistant subpopulation and optionally isolating a compound or agent exhibiting antibacterial activity.

25 10. A process for preparing an agent or compound having antibacterial activity against stationary phase bacteria wherein said agent identified according to the process defined in claim 9 is amplified.

Sub A3 30 11. An antibacterial agent identified or prepared according to the process defined in claim 9 or 10.

35 12. A chemical compound which exhibits antibacterial activity against a phenotypically antibiotic-resistant subpopulation of bacteria as defined in claim. *incomplete*

Sub A4 13. A composition comprising an antibacterial agent or chemical compound as defined in claim 11 or 12 and a

Sub A4
pharmaceutically acceptable excipient or diluent.

5 14. A formulation comprising at least one antibacterial agent having activity against actively growing bacteria and at least one antibacterial agent or chemical compound having activity against a phenotypically antibiotic-resistant subpopulation of stationary phase bacteria as defined in claim 12 or 13 wherein said formulation is presented as a combined preparation for simultaneous, separate or sequential use in the treatment of a bacterial infection.

15 15. An antibacterial agent or chemical compound as defined in claim 12 or 13 for use in the treatment of a bacterial infection.

20 16. Use of an antibacterial agent or chemical compound as defined in claim 12 or 13 in the preparation of a medicament for the treatment of a bacterial infection

25 17. A method of treating of a bacterial infection comprising administering to a patient in need of such therapy an effective amount of an antibacterial agent or chemical compound as defined in claim 12 or 13.

18. A method as claimed in claim 17 further comprising administration of one or more antibacterial agents directed towards actively growing bacteria.

30 Sub A5
19. A formulation, agent, compound, use of method as claimed in any one of claim 14 to 18 where said bacterial infection is characterized by a subpopulation of persistent bacteria which may enter a dormant phase after infection.